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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/423,093 11/01/99 REEVES

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EXAMINER

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ART UNIT	PAPER NUMBER
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1655

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DATE MAILED:

11/15/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>
	09/423,093	REEVES ET AL.
	<b>Examiner</b>	<b>Art Unit</b>
	Bradley L. Sisson	1655

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

1) Responsive to communication(s) filed on 20 October 2000.

2a) This action is FINAL.                    2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

4) Claim(s) 1-42 is/are pending in the application.

4a) Of the above claim(s) 1-15 and 32-42 is/are withdrawn from consideration.

5) Claim(s) \_\_\_\_\_ is/are allowed.

6) Claim(s) 16-31 is/are rejected.

7) Claim(s) \_\_\_\_\_ is/are objected to.

8) Claims \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on \_\_\_\_\_ is/are objected to by the Examiner.

11) The proposed drawing correction filed on \_\_\_\_\_ is: a) approved b) disapproved.

12) The oath or declaration is objected to by the Examiner.

#### Priority under 35 U.S.C. § 119

13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) All b) Some \* c) None of:

1. Certified copies of the priority documents have been received.
2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

14) Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

#### Attachment(s)

15) Notice of References Cited (PTO-892)

16) Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_.

18) Interview Summary (PTO-413) Paper No(s) \_\_\_\_\_.

19) Notice of Informal Patent Application (PTO-152)

20) Other: \_\_\_\_\_

**DETAILED ACTION**

***Election/Restrictions***

1. Applicant's election with traverse of Group III, claims 16-31, in Paper No. 9 is acknowledged. The traversal is on the ground(s) that the Groups are related by common sequences. This is not found persuasive because none of the claims of Group III require any specific sequence that is identified by a SEQ ID NO.

The requirement is still deemed proper and is therefore made FINAL.

***Specification***

2. A substitute specification that includes the claims is required pursuant to 37 CFR 1.125(a) because it is not in proper idiomatic English. A substitute specification in proper idiomatic English and in compliance with 37 CFR 1.52(a) and (b) is required. The substitute specification filed must be accompanied by a statement that it contains no new matter.

A substitute specification filed under 37 CFR 1.125(a) must only contain subject matter from the original specification and any previously entered amendment under 37 CFR 1.121. If the substitute specification contains additional subject matter not of record, the substitute specification must be filed under 37 CFR 1.125(b) and must be accompanied by: 1) a statement that the substitute specification contains no new matter; and 2) a marked-up copy showing the amendments to be made via the substitute specification relative to the specification at the time the substitute specification is filed.

***Claim Rejections - 35 USC § 112***

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 16-31 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The invention, as presently claimed, has sufficient breadth of scope so to encompass the testing of nucleic acids from virtually any bacteria for the presence of encoded O antigens. At page 1 of the specification, it is disclosed that there are at least 166 different versions of this antigen in *E. coli* alone and that there are 46 known variants in *Salmonella enterica*. At page 2, second paragraph, of the specification it is also disclosed that “E. coli O antigen gene clusters for a wide range of E. coli O antigens have been cloned but the O7, O9, O16 and O111 O antigens have been studied in more detail with only O9 and O16 having been fully characterized with regard to nucleotide sequence to date.” At page 3, last paragraph, of the specification it is disclosed that 8 O antigens of *Salmonella enterica* have been characterized. It is not readily apparent, however, how many variants of these various O antigens have been characterized to the level of the nucleotide sequence that encodes same. At page 4, last paragraph, of the specification it is disclosed that “the O antigen of enteropathogenic E. coli strains and the O antigen of Salmonella enterica strains are major virulence factors and are highly polymorphic.” Yet the specification fails to provide an adequate written description of the various nucleic acid sequences of these admittedly highly polymorphic

Art Unit: 1655

antigens. The absence of such basic guidance as to how the invention is to be practiced fails to reasonably suggest that applicant was in possession of the invention at the time the subject application was filed. In support of this position, attention is directed to the decision of *Vas-Cath inc. V. Mahurkar* 19 USPQ2d 1111 (CAFC, 1991):

This court in *Wilder* (and the CCPA before it) clearly recognized, and we hereby reaffirm, that 35 USC 112, first paragraph, requires a “written description of the invention” which is separate and distinct from the enablement requirement. The purpose of the “written description” requirement is broader than to merely explain how to “make and use”; the “applicant must also convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the “written description” inquiry, whatever is now claimed.

5. Claims 16-31 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

6. As set forth above, the specification teaches repeated that the O antigen of bacteria is highly polymorphic and but a few have been fully characterized. The claims have sufficient breadth of scope so to encompass any variant of any bacteria that expresses an O antigen. In order to practice the full scope of the claimed invention, one of skill in the art would have to first identify and develop the requisite starting materials. The situation at hand is analogous to that in *Genentech v. Novo Nordisk A/S* 42 USPQ2d 1001. As set forth in the decision of the Court:

“ ‘[T]o be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation.’ *In re Wright* 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); see also *Amgen Inc. v. Chugai Pharms. Co.*, 927 F. 2d 1200, 1212, 18 USPQ2d 1016, 1026 (Fed Cir. 1991); *In re Fisher*, 427 F. 2d 833, 166 USPQ 18, 24 (CCPA 1970) ([T]he scope of the claims must bear a reasonable

Art Unit: 1655

correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art.').

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"Patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. *See Brenner v. Manson*, 383 U.S. 519, 536, 148 USPQ 689, 696 (1966) (starting, in context of the utility requirement, that 'a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.') Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention.

"It is true . . . that a specification need not disclose what is well known in the art. *See, e.g., Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1385, 231 USPQ 81, 94 (Fed. Cir. 1986). However, that general, oft-repeated statement is merely a rule of supplementation, not a substitute for a basic enabling disclosure. It means that the omission of minor details does not cause a specification to fail to meet the enablement requirement. However, when there is no disclosure of any specific starting material or any of the conditions under which a process can be carried out, undue experimentation is required; there is a failure to meet the enablement requirement that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art. It is the specification, not the knowledge of one skill in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement. This specification provides only a starting point, a direction for further research.

Further, the invention relates directly to performing hybridization reactions. As set forth in Carrico, (US Patent 5,200,313) the extent and specificity of hybridization is affected by the following principal conditions:

1. The purity of the nucleic acid preparation.
2. Base compositions of the probe - G-C base pairs will exhibit greater thermal stability

than A-T or A-U base pairs. Thus, hybridizations involving higher G-C content will be stable at higher temperatures.

Art Unit: 1655

3. Length of homologous base sequences- Any short sequence of bases (e.g., less than 6 bases), has a high degree of probability of being present in many nucleic acids. Thus, little or no specificity can be attained in hybridizations involving such short sequences. From a practical standpoint, a homologous probe sequence will often be between 300 and 1000 nucleotides.

4. Ionic strength- The rate of reannealing increases as the ionic strength of the incubation solution increases. Thermal stability of hybrids also increases.

5. Incubation temperature- Optimal reannealing occurs at a temperature about 25 - 30 °C below the melting temperature for a given duplex. Incubation at temperatures significantly below the optimum allows less related base sequences to hybridize.

6. Nucleic acid concentration and incubation time- Normally, to drive the reaction towards hybridization, one of the hybridizable sample nucleic acid or probe nucleic acid will be present in excess, usually 100 fold excess or greater.

7. Denaturing reagents- The presence of hydrogen bond-disrupting agents, such as formaldehyde and urea, increases the stringency of hybridization.

8. Incubation- The longer the incubation time, the more complete will be the hybridization.

9. Volume exclusion agents- The presence of these agents, as exemplified by dextran and dextran sulfate, are thought to increase the effective concentrations of the hybridizing elements thereby increasing the rate of resulting hybridizations.

Further, subjecting the resultant hybridization product to repeated washes or rinses in heated solutions will remove non-hybridized probe. The use of solutions of decreasing ionic

Art Unit: 1655

strength, and increasing temperature, e.g., 0.1X SSC for 30 minutes at 65 °C, will, with increasing effectiveness, remove non-fully complementary hybridization products.

Upon review of the specification, it is not readily apparent how the skilled artisan is to resolve these issues. Furthermore, the claims do not recite the required method steps that would permit such a file level of detection.

In view of the highly variable reaction conditions that the skilled artisan would need to utilize in order to detect any bacteria that is expressing any variant of any O antigen, and given the few starting materials and reaction conditions enumerated by the specification of the subject application, the skilled artisan would have to resort to many years of experimentation with little if any reasonable expectation of success. Such shifting of the burden of enablement from applicant to the public is unfair as the level of experimentation required is undue.

In view of the reasons given above, and in the absence of convincing evidence to the contrary, the specification has not been found to enable the claimed invention.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 16-31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

9. Claims 16-31 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: Those steps which will ensure the detection of specific

Art Unit: 1655

bacteria to the exclusion of non-target bacteria. While the claims recite that the conditions are such that at least one probe will hybridize specifically to its target, such does not preclude non-target sequences will also hybridize. It is noted that under hybridization reactions, the strands anneal in relationship to the stringency of the hybridization reaction conditions and the degree of complementarity, or coefficient of association. Accordingly, even under non-stringent conditions fully complementary sequences will still bind to their target as well as permitting non-fully complementary sequences to hybridize to non-target sequences as well.

***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bradley L. Sisson whose telephone number is (703) 308-3978. The examiner can normally be reached on 6:30 a.m. to 5 p.m., Monday through Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3592 for regular communications and (703) 308-0294 for After Final communications.

Art Unit: 1655

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.



Bradley L. Sisson  
Primary Examiner  
Art Unit 1655

BLS  
November 14, 2000